Paper No. 18

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte WAYNE E. CHILDERS, JR.,
HORACE FLETCHER, III,
MAGID A. ABOU-GHARBIA, and
JOHN P. YARDLEY

Appeal No. 2003-0890
Application No. 09/706,683

ON BRIEF

WINTERS, WILLIAM F. SMITH and ADAMS, Administrative Patent Judges.

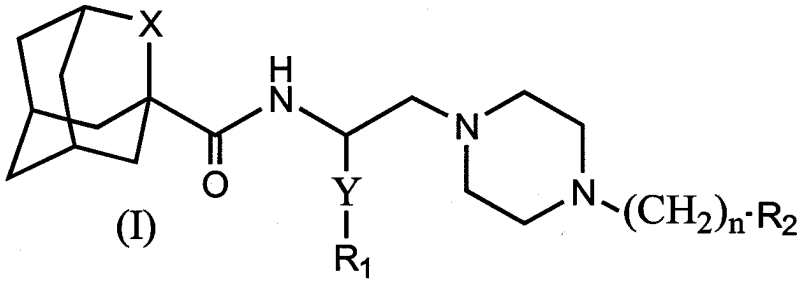
WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-3, 16, and 27-30. Claims 4, 7-12, 14, and 15 are pending but have been objected to by the examiner. These are the only claims pending in the application.

Claims 1 and 16 are representative of the subject matter on appeal and read as follows:

1. A compound of the formula (I):



(I)

X is selected from $-CH_2-$ or a chemical bond;

Y is selected from $-(CH_2)_m-$ or $-(CH_2)-O-(CH_2)-$;

m is selected from the integer 0 or 1;

n is selected from the integer 0 or 1;

R_1 and R_2 are independently selected from the group consisting of aryl, monocyclic heteroaryl having 5 – 6 ring atoms of which 1-3 ring atoms are independently selected from the group consisting of N, S and O, and bicyclic heteroaryl having a phenyl ring fused to a monocyclic heteroaryl ring as defined above, optionally substituted with F, Cl, Br, I, -OH, $-NH_2$, $-CO_2H$, $-CO_2-C_1-C_6$ alkyl, -CN, $-NO_2$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 perhaloalkyl, OR_3, or C_1-C_6 perhaloalkoxy;

R_3 is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_6-C_{10} aryl, monocyclic heteroaryl having 5 –6 ring atoms of which 1-3 ring atoms are independently selected from the group consisting of N, S and O, and bicyclic heteroaryl having a phenyl ring fused to a monocyclic heteroaryl ring as defined above, C_7-C_{14} aralkyl, and mono or bicyclic heteroaralkyl consisting of a C_1-C_4 alkyl having a substituent which is a mono or bicyclic heteroaryl as defined above, where the aryl or heteroaryl group is optionally substituted with one to three substituents independently selected from the group consisting of F, Cl, Br, I, CN, $-NH_2$, $-NO_2$, -OH, alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 perhaloalkyl, C_1-C_6 alkoxy, and C_1-C_6 perhaloalkoxy;

and the optical isomers or a pharmaceutically acceptable salt thereof.

16. A method for treating stroke comprising administering a therapeutically effective amount of a compound of Claim 1 or a pharmaceutical salt thereof, to a patient in need of said treatment.

The references relied upon by the examiner are:

Abou-Gharbia et al. (Abou-Gharbia)	5,254,552	Oct. 19, 1993
Cliffe	5,420,278	May 30, 1995

Claims 1, 2, 16, and 27 through 30 stand rejected under 35 U.S.C. § 112, first paragraph (enablement). Claims 1 through 3 stand rejected under 35 U.S.C. § 103(a). As evidence of obviousness, the examiner relies upon Abou-Gharbia and Cliffe. We reverse the enablement rejection and affirm the obviousness rejection.

Background

As seen from claims 1 and 16, the claimed invention is directed to a family of compounds having a specified formula and their use in treating stroke victims. The claimed compounds are stated to have activity as serotonin 5-HT_{1A} agonists, partial agonists and antagonists. Specification, page 3.

In regard to making the compounds set forth in claim 1 on appeal, appellants state "[t]he compound of formula I can be prepared by conventional chemical methods which are well known to those skilled in the art of chemistry using chemicals that are either commercially available or readily prepared following standard literature procedures." Specification, page 8.

Discussion

1. Enablement.

The examiner raises the issue as to whether one skilled in the art would be able to use the compounds encompassed by claims 1 through 3 that have "heteroaryls both mono- and bicyclic at every R variable." Examiner's Answer, page 4. The examiner explains that the specification states that some of the claimed compounds are partial agonists while others are antagonists. Id., pages 4-5. The examiner concludes "[i]t remains the examiner's position that the amount of guidance presented in the specification as to which (het-substituted) compounds having the necessary 5-HT_{1A} agonist and/or antagonist activity is minimal and consequently applicants' disclosure provides merely an invitation of those of ordinary skill in the art to determine which compounds have agonist activity, and which are antagonistic or have a mixed profile of activity." Id., page 5.

In considering the issue, we note that the examiner has not raised any objection to the claims in terms of how to make, but, rather, the examiner's concern is directed to the so-called heteroaryl compounds in regard to the how to use requirement of this section of the statute. The examiner is concerned that the specification does not provide guidance as to which compounds have 5-HT_{1A} agonist and/or antagonist activity. If the examiner's concern is based upon the thought that a person of skill in the art must be able to assign agonist and/or antagonist activity to each compound included in the rejected claims only by analysis of the structure of the compound, the rejection is based upon the wrong legal standard.

As set forth in PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996):

> In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. See, e.g., In re Goodman, 11 F.3d 1046, 1050-52, 29 USPQ2d 2010, 2013-15 (Fed. Cir. 1993); Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d. 1200, 1212-14, 18 USPQ2d 1016, 1026-28 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991); In re Vaeck, 947 F.2d at 496, 20 USPQ2d at 1445. Enablement is lacking in those cases, the court has explained, because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. But the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." Atlas Powder Co., v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). The Patent and Trademark Office Board of Appeals summarized the point well when it stated:
>
> > The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.
>
> Ex parte Jackson, 217 USPQ 804, 807 (1982).

Here, it is not unreasonable to expect that a person skilled in the art would need to perform some experimentation in order to determine the activity profile of a given compound set forth in the rejected claims. The key here is whether ascertaining the activity profile of a given compound would require undue experimentation instead of being performed in a routine manner. The specification describes an assay that those

skilled in the art would use in order to determine the activity profile of a given compound. Id., pages 18-19. Under these circumstances, it was the examiner's responsibility to set forth a fact-based explanation as to why use of such an assay to determine the activity profile of a given compound would require undue experimentation. We do not have such an analysis.

The enablement rejection is reversed.

2. Obviousness.

The examiner relies upon Abou-Gharbia as describing compounds which bind the 5-HT_{1A} receptor. Abou-Gharbia, column 3, lines 5-8. The examiner states that Abou-Gharbia describes at least two compounds which differ from those required by claims 1-3 on appeal in the closest approximation by "lacking instant Y-R1 group." Examiner's Answer, page 7. The examiner specifically points to two compounds described at column 2, lines 22-26 of Abou-Gharbia, i.e.,

N-[2-[4-(2-pyrimidinyl)-1-piperazinyl]ethyl]tricyclo[3.3.1.1^{3,7}]decane-1-carboxamide;
N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]tricyclo[3.3.1.1^{3,7}]decane-1-carboxamide;

Id. In other words, in the closest approximation the two Abou-Gharbia compounds identified by the examiner contain an ethyl bridging moiety while the compounds required by claims 1-3 can have an ethyl bridging moiety substituted by aryl, e.g., phenyl (Y = $-(CH_2)_m-$ with m = 0 and R_1 = aryl).

The examiner relies upon Cliffe for its description of compounds similar to those of claim 1 on appeal and those described in Abou-Gharbia. Importantly, the Cliffe compounds may have the corresponding ethyl bridging moiety substituted by phenyl. See compounds of formula I of Cliffe where n = 1, R^2 is hydrogen and R^3 is an aryl radical. The compounds described in Cliffe also bind to 5-HT_{1A} receptors. Id., column 7, lines 28-44. The compounds of Cliffe may also be carboxamides as are the compounds of claims 1-3 (X = $-NR^4COR^6$).

The examiner has concluded that it would have been obvious to one of ordinary skill in the art to form compounds that are structurally similar to those described in Abou-Gharbia differing in that the ethyl bridging moiety of the compounds of Abou-Gharbia are substituted by phenyl as described in Cliffe. Examiner's Answer, page 8. The examiner reasons that one would expect those compounds to also exhibit the common activity as being a serotonin antagonist, i.e., bind to 5-HT_{1A} receptor. We agree.

As explained in In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979), "[a]n obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make the compound, in the expectation that compounds similar in structure will have similar properties" (citations omitted). Here, the applied prior art establishes that one of ordinary skill in the art would have reasonably expected the compounds of Abou-Gharbia having the ethyl bridging moiety modified by a phenyl group would continue to exhibit the property of binding to the 5-HT_{1A} receptor. This is seen from the Cliffe reference which describes compounds

similar to those of Abu-Gharbia and those set forth in claims 1-3 on appeal in which the corresponding ethyl bridging moiety is substituted by phenyl and exhibit the property of binding to 5-HT_{1A} receptors.

Appellants argue that the examiner's rejection is based upon hindsight. We disagree. As set forth above, case law establishes that those of ordinary skill in the art are "motivated" to make structurally similar compounds with the expectation that the compounds similar in structure will have similar properties. In arguing the examiner's rejection, appellants focus upon the "most preferred reference compounds." Appeal Brief, pages 7-8. Be that as it may, a reference must be read in its entirety and not be subject to a reading limited to the preferred embodiments. In re Mills, 470 F.2d 649, 651, 176 USPQ 196, 198 (CCPA 1972).

The second aspect of appellants' argument is that the applied prior art does not teach one how to make the compounds of the present invention. Appeal Brief, page 10. Appellants are of course correct that the applied prior art must be enabling. In re Payne, at 314, 203 USPQ at 255 ("References relied upon to support a rejection under 35 USC § 103 must provide an enabling disclosure, i.e., they must place the claimed invention in the possession of the public."). Specifically, appellants only argue "compounds which have different structures require different starting materials and, even when the structures seem very similar, an entirely different synthesis route may be needed." Appeal Brief, page 10. Appellants do not analyze the procedures set forth in Abou-Gharbia or Cliffe and explain why those procedures would not enable one to make the claimed compounds as proposed by the examiner. We note that Abou-Gharbia and

Cliffe are United States patents and as such, are presumed to be valid. 35 U.S.C. § 282. Thus, the two patents are presumed to be enabling of the claimed subject matter. Clearly appellants' unsupported assertion that the applied prior art is not enabling is insufficient.

To summarize, the examiner's rejection of claims 1, 2, 16, and 27 through 30 under 35 U.S.C. § 112, first paragraph (enablement), is reversed, and the examiner's rejection of claims 1 through 3 under 35 U.S.C. § 103(a) is affirmed.

The decision of the examiner is affirmed-in-part.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

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Sherman D. Winters	)
Administrative Patent Judge	)
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	) BOARD OF PATENT
William F. Smith	)
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